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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,085	04/18/2005	Thierry Massfelder	BJS-3665-133	9193

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EXAMINER	
GUSSOW, ANNE	
ART UNIT	PAPER NUMBER
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/24/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,085	MASSFELDER ET AL.	
	Examiner	Art Unit	
	Anne M. Gussow	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-37* is/are pending in the application.

4a) Of the above claim(s) *27-30,36 and 37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-26 and 31-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 April 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *September 21, 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of Group IV, claims 32-35, in the reply filed on December 13, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claim 31 (Group III) has been rejoined with claims 32-35 (Group IV) for reading on the anti-PTHrP antibody. Thus, the new groups are as follows:

Group I: Claims 27, 28, and 30 drawn to a method for using PTH or PTHrP peptides.

Group II: Claim 29 drawn to a method of using a non-peptide antagonist.

Group III: Claims 31-35 drawn to a method of using an anti-PTHrP antibody.

Group IV: Claim 36 drawn to a method of using a PTHrP antagonist by binding to mRNA or a gene.

Group V: Claim 37 drawn to a method of using a PTHrP antisense oligonucleotide.

3. Claims 27-30 and 36-37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on December 13, 2006.

4. Claims 17-26 and 31-35 are under examination.

Specification

5. The disclosure is objected to because of the following informalities: Typographical errors, for example, on page 16 last line to page 17 line 1, Figure "14" should read Figure "17" and on page 32 line 4 "hte" should be "the".

Appropriate correction is required throughout.

6. The use of the trademark RedTaq™ (page 19, line 19) and Lipofectamine™ (page 21 line 2) have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

The trademark symbols are not present in the specification. Appropriate correction is requested throughout.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 17-26 and 31-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 is indefinite for reciting "an effective dose of a PTHrP antagonist." It is not clear if the effective dose refers to the dose necessary to antagonize PTHrP or the dose necessary to prevent or cure kidney cancer.

The phrase "an effective amount" has been held to be indefinite when the claim fails to state the function which is to be achieved and more than one effect can be implied from the specification or the relevant art (See MPEP 2173.05(c)).

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 17-26 and 31-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a subject with kidney cancer by administering an anti-PTHrP antibody which reduces the size of tumors ~~in an animal model~~, does not reasonably provide enablement for preventing or curing kidney cancer in a subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

RT 1/14/07

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 1 12, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988).

> Wands states on page 1404,
> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

Applicant discloses a method for treating a kidney cancer in a mouse model comprising the administration to a subject of an anti-PTHrP antibody. The specification does not provide any teachings of the broadly claimed prophylaxis of a kidney cancer, how to determine the individuals who will develop a kidney cancer, nor how to effectively prevent said particular cancer type before occurrence, nor does the specification teach the how to predict when a cancer would occur in any individual or the optimal time before such a occurrence to administer the composition of the instant invention. Thus, one of skill in the art would not be able to use the composition of the invention as a vaccine without undertaking to determine how to select for individuals which will develop a particular cancer type before the said cancer occurs in the individual.

Additionally, the specification does not disclose the treatment of metastatic developments in kidney cancer. Drucker (Cancer Treatment Reviews, 2005, Vol. 31, pages 536-545) teaches median survival of patients with advanced renal cell carcinoma

as less than 1 year (page 536, 2nd column). Drucker also teaches new therapies to improve the response to metastatic lesions including interferon-α, IL-2, and an antibody to VEGF resulted in mixed and indirect results (pages 540-542). In the case of interferon-α, improvement was seen in combination with nephrectomy but not with interferon-a alone (page 540, 1st column). Thus, one of skill in the art would not be able to treat metastatic developments in kidney cancer without determining the efficacy of an anti-PTHrP antibody against metastasis.

Regarding the development of a prophylactic immune response against cancer it is noted that the abstract of Wheeler (Salud p'ublica de M'exico, (1997 Jul-Aug Vol. 39 No. 4 pages 283-7) teaches that a cancer vaccine against human papillomavirus for the treatment of cervical cancer requires not only the activation of antigens and overcoming the host response, but the generation of high levels of T and B memory cells; and the persistence of antigens. The instant specification has not provided any teachings regarding the persistence of the tumor antigens in an individual who has yet to develop a specific type of cancer. Further, Efferson et al. (Anticancer research, 2005, Vol. 25, pp. 715-24) teach that efficient induction of memory cells is hindered by the lack of information about the relationship between TCR stimulation and the cytokines required for Ag-specific memory CD8+ cells and proliferation and survival. The instant specification has not provided any evidence that adequate levels of T and B memory cells would persist in an immunized individual who has not developed a cancer. Bachman et al (Journal of Immunology, 2005, Vol. 175, pp. 4677-4685) teach that memory T cells are not a homogeneous population and can be divided into central

memory T cells with a substantial capacity for recall proliferation and effector memory T cells with limited recall proliferation capacity. Bachman et al teach that the protective capacity of the different subpopulations of memory T cells vary, and the generation of the subpopulations is influenced by the nature and route of immune challenge. These references serve to demonstrate that the prior art is not mature with respect to how to elicit an effective prophylactic memory cell response that will persist in an individual not harboring a tumor cells and which would function to protect said individual from tumor cell development. Because the specification does not address the issues regarding how to elicit an effective memory cell response from the administration of the claimed compositions, and no objective evidence or working examples have been provided, one of skill in the art would be subject to undue experimentation in order to make and use the claimed composition as protection against a kidney cancer.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 17-21, 23-26, and 31-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ogata, et al. (EP 1 197 225 A1, published April 17, 2002) in view of Burton, et al. (Biochemical and Biophysical Research Communications, 1990. Vol. 167 No. 3 pages 1134-1138).

The claims recite a method for treating preventatively or curatively a kidney cancer comprising administration to a subject an effective dose of a PTHrP antagonist wherein the antagonist binds to the PTHrP receptor and inhibits PTHrP binding, and is a humanized monoclonal or polyclonal anti-PTHrP antibody, and wherein the kidney cancer is a solid malignant tumor selected from the group consisting of papillary carcinoma (chromophiles), chromophobe cell carcinoma, Bellini carcinoma, clear cell carcinoma, or unclassified renal cell carcinoma.

Ogata, et al. teach a method for treating hypercalcemia by administering a humanized monoclonal anti-PTHrP antibody to a rat cancer model (page 13, example 4) in which the PTHrP antibody binds to the PTHrP receptor (page 5, paragraph 37). Ogata, et al. do not teach treating kidney cancer. This deficiency is made up for the in the teachings of Burton, et al.

Burton, et al. teach that PTHrP antiserum specifically inhibited the growth of a human renal cell carcinoma cell line *in vitro* (figure 3, table 1 and page 1137, 2nd paragraph).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the anti-PTHrP antibody of Ogata, et al. to treat kidney cancer as taught by Burton, et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have treated kidney cancer with the antibody of Ogata, et al. because Ogata et al. teach that hypercalcemia is a syndrome associated with a large number of malignant tumors and the anti-PTHrP antibody reduced the symptoms of hypercalcemia. Additionally, Burton, et al. teach that inhibition of PTHrP reduced the growth of renal cancer cells but not ROS 17/2.8 cells (a rat osteoblastic osteocarcinoma cell line which possesses PTH receptors) or bovine adrenal medullary cells (page 1137, 2nd paragraph). Thus, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to have treated kidney cancer in view of Burton, et al. with the antibody of Ogata, et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made, as evidenced by the references.

Conclusion

13. No claims are allowed.

14. The claims recite a method for using an antibody against PTHrP. The specification discloses three antibodies that are publicly available (page 26 line 30 to page 27 line 3), thus no deposit is required for the anti-PTHrP antibody.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne M. Gussow whose telephone number is (571) 272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow

January 10, 2007

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER